lead. He also found that, even after going through the intervening materials, the X-rays were not deflected. When he reached through the path of the X-rays, he was surprised to see that the bones of his hand cast a clear shadow on the fluorescent screen.

In December of 1895, Röntgen sent a communication describing his findings to *Sitzungsberichte der Wurzburger Physikalischen-Medicinischen Gesellschaft*. The news of this discovery quickly spread around the world, and this communication was translated and reprinted in many journals, including *Nature* and *Science*.

The implications of Röntgen's discovery were quickly recognized. In the spring of 1896, two physicians at the Dartmouth Medical School used the X-rays to diagnose bone fractures in a man's wrist. However, the impact of X-rays was not limited to medical applications. The discovery of X-rays marked the beginning of modern physics, and in 1901 Röntgen was awarded the first Nobel prize in physics. For structural biologists, the discovery of X-rays gave them one of the most important tools for investigating the architecture of biological macromolecules.

Hwa-ping Feng

A hormone receptor springs into action

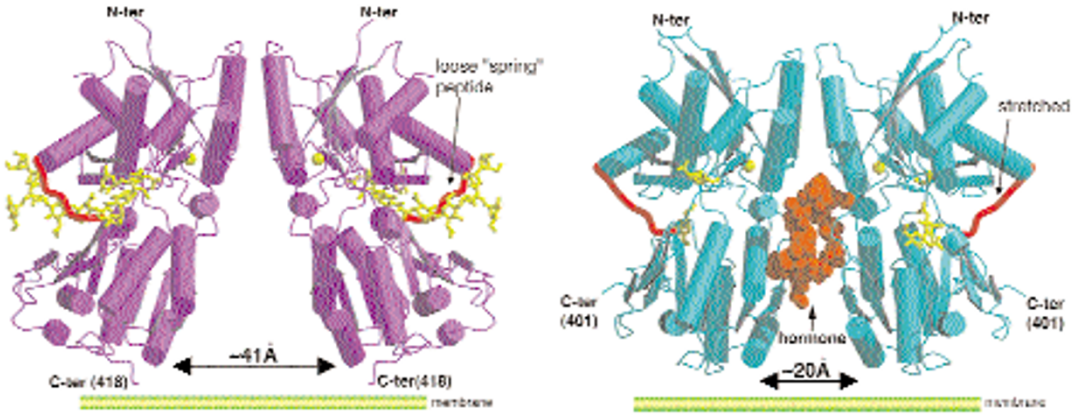
Although high blood pressure is a common condition, its molecular basis is not well understood. Among the key players in blood pressure and fluid regulation are the natriuretic peptide hormones (ANP, BNP and CNP) — short, homologous peptides that generally decrease blood pressure and increase salt excretion. Understanding the pathways they activate may help in developing treatments for various cardiac pathologies related to hypertension.

The most abundant receptor for the natriuretic peptides is NPR-C; it can bind to all three hormones and is thought to be involved in clearance of the peptides and regulation of their local concentration as well as signaling. The structural basis for how hormone binding affects this receptor and leads to downstream events remains unclear.

K. C. Garcia and colleagues (He *et al.*, *Science* **293**, 1657–1662; 2001) have recently determined the X-ray crystal structure of the glycosylated extracellular domain of NPR-C, by itself (left) and in complex with the peptide hormone CNP (right). The basic structure of each monomer in the dimeric receptor resembles that seen in the previously published structure of the related NPR-A. However, the structure of NPR-C reveals that its dimerization is mediated through the N-terminal domain, with a single peptide hormone binding at the dimer interface. In contrast, the previous structure shows NPR-A dimerizing through its C-terminal domain and predicts two binding sites per dimer. Based on isothermal titration calorimetry experiments, He *et al.* show that the stoichiometry of the receptor: hormone binding is 2:1, supporting the argument that their NPR-C structure represents the physiologically relevant dimer.

How does hormone binding to these receptors lead to signal transduction? Comparison of the structures with and without peptide reveals that there is a large domain movement in NPR-C upon hormone binding, bringing the C-terminal domains of the dimer closer together by ~20 Å and widening the angle between the N- and C-terminal domains. Interestingly, a linker peptide (red) between the two domains, in concert with the glycan (yellow), appears to act as a 'molecular spring', constraining the receptor in the closed, unbound conformation and stretching out in the open, bound form. In the absence of hormone, this peptide forms several hydrogen bonds with the carbohydrate and the rest of the protein. Upon hormone binding, the peptide is stretched by ~2.5 Å, losing most of these contacts, and the glycan becomes largely disordered. This spring-like mechanism may be important for the large domain movement associated with hormone binding. How this in turn activates downstream signaling has yet to be determined, but the structures by He *et al.* provide a key step toward understanding this pathway and designing potential treatments for cardiovascular diseases.

Julie Hollien



Modified with permission from He *et al*.